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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,531	03/30/2005	Paul Dent	ON/4-32419A	8871

1095 7590 11/07/2008

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
11/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,531	DENT ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *17-22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on August 6, 2008.

Status of Claims

Claims 17-22 are currently pending and are the subject of this office action.

Claims 17-22 are presently under examination.

Priority

The present application is a 371 of PCT/IB03/01418 filed on 04/04/2003, and claims priority to provisional application No. 60/371,330 filed on 04/10/2002.

Response to Arguments

This is in response to applicant's arguments, filed on August 6, 2008.

Claims rejected under 35 USC 103 (a)

Applicant's arguments have been fully considered but are not persuasive.

Applicant argues that the prior art cited (Yu et. al. ,Blood, Vol. 98(11), 2001:146a, abstract 615, cited by applicant, cited in prior office action) does not teach that the synergistic mixture of Flavopiridol and Imatinib (STI571) treats leukemia that is resistant to Imatinib. However Yu et. al. teach that : "Exposure of K562 or LAMA-84 cells (Human leukemia cell lines) to 200 nM STI571 (Imatinib) for 48 hs only , minimally induced apoptosis (e.g. less than 10%), manifested by the characteristic morphologic

features or the appearance of hypodiploid cells by flow cytometry. However, when cells were co-incubated with a marginally toxic and pharmacologically achievable concentration of Flavopiridol (i.e. 150 nM), a striking increase in mitochondrial damage (e.g., loss of mitochondrial membrane potential) was noted, accompanied by a marked increase in activation of procaspases-3 and -8, cleavage of Bid, PARP degradation, and the morphologic features of apoptosis (i.e. in more than 60% of the cells).

This clearly indicates that the leukemia cells did not originally respond to the treatment of Imatinib (STI571) alone, meaning that the cells were resistant to Imatinib. But then, they responded well to the co-treatment with Imatinib and Flavopiridol.

Rejection under 35 USC 103(a) is maintained.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 17-22 rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et. al. (Blood, Vol. 98(11), 2001:146a, abstract 615, cited by applicant, cited in prior office action).

Claims 17-22 recite a method of treating Bcr/Abl-positive leukemia resistant to STI571 (Glivec or Imatinib), comprising administering to a patient in need thereof a combination of a) flavopiridol and b) STI571 in the form of a pharmaceutically

acceptable salt, and optionally at least one pharmaceutically acceptable carrier, in a synergistically effective molar ratio (flavopiridol/STI571) range of 1:1 to 1:10.

Yu et. al describe a synergistic combination of flavopiridol and STI571, in a 1:1.3 ratio, to induce mitochondrial damage and apoptosis in Bcr/Abl-positive leukemia cells resistant to STI571 (see entire abstract).

At the time of the invention it would have been prima facie obvious to for a person of ordinary skill in the art to apply the teachings of Yu et. al. (the synergistic effect of flavopiridol and b) STI571 in Bcr/Abl-positive leukemia cells resistant to STI571) to develop a method of treating Bcr/Abl-positive leukemia resistant to STI57, thus resulting in the practice of claims 17-22 with a reasonable expectation of success.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/ /Brandon J Fetterolf/

Examiner, Art Unit 1612 Primary Examiner, Art Unit 1642
November 1, 2008